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DR. ERNEST LITTLE
Remington Medalist 1949

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OUR COVER

DR. ERNEST LITTLE

Remington Medalist 1949

THE selection of Dr. Ernest Little to receive the Remington Medal adds still another distinguished name to that list of twenty six other pharmaceutical leaders who have been similarly honored over the years. This medal has come to be recognized as Pharmacy's highest honor and to merit receiving it is, in itself, an accomplishment and a sign of most distinguished service.

Dr. Little, although not a pharmacist by training, has devoted his life in the interest of the profession. During his many years as Dean of the School of Pharmacy, now a part of Rutgers University, he came to be recognized and respected for his sound judgment and courageous leadership, not only among the pharmacists of New Jersey but throughout the entire nation. It was quite natural that he should be chosen to fill many positions of trust and great responsibility in the field of pharmacy. Dr. Little has served as president of the American Association of Colleges of Pharmacy and as chairman of its Executive Committee. He was for several years a member of the American Council on Pharmaceutical Education and contributed much toward the raising of educational standards. As a former president and a present member of the Board of Grants, Dr. Little has been an important member of the American Foundation for Pharmaceutical Education. Dr. Little just completed a term as president of the American Pharmaceutical Association and he is now serving as a member of its Council.

Although Dr. Little retired from the deanship at Rutgers a few years ago, he has maintained his deep interest in pharmacy and still teaches pharmacy students in his chosen field, chemistry. Many have been his honors and great is the esteem with which all regard him.

Our compliments and congratulations to Dr. Ernest Little for a recognition and honor that is well deserved.

E D I T O R I A L

THE ELIXIR OF LIFE?

TO say that interest in cortisone or compound E as well as ACTH has reached a feverish pitch would be almost an understatement. Probably no discovery since that of penicillin has so intrigued the scientist and layman alike, for it may well be that cortisone or some related steroid shall become the portal of approach to a new understanding of the whole process of degenerative diseases. If this should prove to be the case, then truly it would outrank penicillin as a major discovery.

The degenerative diseases, today, rank as the number one group that still defies an effective therapeutic approach. True, we have some little knowledge of how to delay these seemingly irreversible processes and how to palliate their damaging action on heart, kidneys, blood vessels, other organs and tissues. In general, however, the therapy available is quite unsatisfactory, and prophylactic measures offer but small encouragement to those who have the determination to follow rigidly the dietary measures, exercises, etc. that such incur. There seems little doubt that degenerative processes can be initiated or at least accelerated by emotional stress, and modern civilization is surely not conducive to a serenity of mind. With life-expectancy now about 70 years, degenerative disease is likely to be, or eventually become, an immediate problem for us all.

There are those who claim that the process of aging is absolute, that it is an intrinsic property of all tissue and that it cannot be arrested or reversed. This view fails to explain the wide variations known to exist in the life-span of different species and even within a single species. Why is it that some men are actually old at forty while others are still dynamically alive and active at seventy? The answer must be chemical, for no other explanation fits the facts. Obviously heredity, environment, diet, etc. all play a part but only in that they influence the total biochemistry of the organism. Some people have been known to grow old prematurely and then later appear to grow younger! Is this not a seeming reversal of degenerative processes?

There seems to be no fundamental reason why an animal such as man might not live indefinitely, provided the complex changes that take place leading to senility are arrested. This is a challenging task, it is true, and it may well be that none of us will survive long enough to enjoy the fruits of its accomplishments, but is it really so impossible? Today, we accept atomic energy which we have accumulated in such amounts that it is likely we could blow the world apart. Interplanetary space ships are not too far distant, and already we can fly around the world and be back before we started (sun time). Not only can we televise events through space, but we do so in natural color. The power of *psi*, including preconception, has been proven and this without any known physical basis of explanation. Surely the chemical processes of aging cannot long defy the mind of man who can do these things.

It is our firm conviction that this great accomplishment still awaits us. Already we have seen many manifestations of an increased longevity. Life-expectancy, today, is seemingly growing with each passing year, although most of the progress leading to this increase may be traced to our conquest of infectious diseases affecting the young. Many years may pass before scientists learn the intricate secrets of aging, but the problem shall be solved.

On the basis of the changes we have seen in just a few decades can we say with assurance that this thing is impossible?

Throughout all man's history he has sought avidly for the means to attain everlasting life. When such is at his disposal, he will probably consider death with little fear. In fact, it often may be sought by those who tire of the persistence of life. Human nature, alone, seems to be changeless, for we ceased to regard highly that which we possess.

L. F. Tice

EVALUATING THE BACTERICIDAL EFFICIENCIES OF FREE IODINE AND AVAILABLE CHLORINE BY THE "SEMI-MICRO" METHOD

By Louis Gershenfeld and Joseph A. Palisi *

A "Semi-Micro" Method was reported by Klarmann and Wright for testing the bactericidal efficiency of quaternary ammonium compounds (1). This technique retains the fundamental principles of the F. D. A. method (2) used in the testing of these compounds. In the semi-micro technique, the entire medication mixture, measuring one-tenth the total volume of the corresponding mixture under the conditions of the F. D. A. Method, is cultured and incubated. For reasons of time and economy, only ten minute contact periods are employed. Salle and co-workers (3) found that the ten minute period of exposure is probably the maximal time for effective germicidal action on a cut surface or mucous membrane. Klarmann (4) stated that under the conditions of the F. D. A. testing method, there exists (or is presumed to exist) one definite concentration of phenol and one of the disinfectant substances under test producing the death of the inoculum at the same time, namely 10 minutes.

Purpose

This investigation was undertaken to determine and evaluate the bactericidal efficiencies of free iodine and available chlorine by the Klarmann "Semi-Micro" Method and also by a modified F. D. A. Technique.

Procedure

(A) The test organisms employed were: *Salmonella (E.) typhosa* (Hopkins strain) and *Staphylococcus aureus* (No. 209).

Stock cultures of the organisms were kept on F. D. A. agar. The organisms were transferred daily, using one 4 mm. loopful of inoculum and incubated in the medium, as outlined in (B). Fresh transplants from the stock cultures were made every three weeks.

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

(B) The medium was prepared as follows:

Bacto Peptone	10 Gm.
Sodium Chloride	5 Gm.
Bacto Beef Extract	5 Gm.
Distilled Water qs.	1000 cc.

The mixture was boiled for 20 minutes and made up to original volume with distilled water. It was then filtered, tubed (10 cc. to each tube) and sterilized at 121.3°C. (15 pounds pressure) for 30 minutes. The pH of the medium after sterilization was 6.8—7.0.

(C) The test solutions used were:

Iodine Tincture U. S. P. (5) and Aqueous Sodium Hypochlorite Solution (2 percent available chlorine).

(D) The technique of the "Semi-Micro" Method (1) was as follows:

Five hundredths cc. of a 24 hour broth culture of the test organism was pipetted into the bottom of sterile 25 x 150 mm. test tubes. This first step in the procedure was performed with care so that the pipette did not touch the walls of the test tube. The tubes were placed in a water bath at 20°C. Then 0.5 cc. of different dilutions of the disinfectant under test, which had also been kept in a water bath at 20°C., was added to the tubes and thoroughly mixed with the culture. Ten minutes after adding the dilutions of the disinfectant, 2 cc. of 0.1 N. sodium thiosulfate solution and 10 cc. of culture medium were poured into the tubes employing aseptic precautions. All tubes were then incubated for 48 hours at 37°C.

This method was also employed for the phenol controls, omitting the addition of 2 cc. of 0.1 N sodium thiosulfate.

(E) The following modified F. D. A. technique was also employed:

Five cc. of diluted disinfectant were added to sterile 25 x 150 mm. test tubes. The tubes were then placed in a water bath at 20°C. One-half cc. of a 24 hour broth culture of the test organism, which had also been kept in a water bath at 20°C., was added to

each tube and thoroughly mixed with the disinfectant dilutions. Ten minutes after adding the organisms, 2 cc. of 0.1 N sodium thiosulfate solution was poured into the tube and one 4 mm. loopful of the mixture was transferred to the subculture tube containing 10 cc. of culture medium. All tubes were incubated for 48 hours at 37°C.

This method was also employed for the phenol controls, omitting the addition of 2 cc. of 0.1 N sodium thiosulfate solution.

Findings

With the "Semi-Micro" Method, a 1:4000 solution of available chlorine killed *Salmonella (E.) typhosa* in 10 minutes, and a 1:5000 solution of available chlorine killed *Staphylococcus aureus* in 10 minutes. See table 1.

TABLE 1

BACTERICIDAL EFFICIENCY OF AVAILABLE CHLORINE EMPLOYING THE "SEMI-MICRO" METHOD AT 20° C.

	Salmonella (E.) typhosa	*Staphylococcus aureus*
Available Chlorine	10 minute contact	10 minute contact
1:3000	0	0
1:4000	0	0
1:5000	+	0
1:6000	+	+
1:7000	+	+
Phenol Control		
1:70	0	0
1:80	0	0
1:90	0	+
1:100	+	+
1:110	+	+

0 = No growth after 48 hours. + = Growth after 48 hours.

With the "Semi-Micro" Method, a 1:8000 solution of free iodine killed *Salmonella (E.) typhosa* in 10 minutes, and a 1:6000 solution of free iodine killed *Staphylococcus aureus* in 10 minutes. See table 2.

TABLE 2

BACTERICIDAL EFFICIENCY OF FREE IODINE EMPLOYING THE "SEMI-MICRO" METHOD AT 20° C.

Free Iodine	*Salmonella (E.) typhosa* 10 minute contact	*Staphylococcus aureus* 10 minute contact
1:6000	0	0
1:7000	0	+
1:8000	0	+
1:9000	+	+
1:10000	+	+
Phenol Control		
1:70	0	0
1:80	0	0
1:90	0	+
1:100	+	+
1:110	+	+

0 = No growth after 48 hours. + = Growth after 48 hours.

With a modified F. D. A. method, a 1:16000 solution of available chlorine killed *Salmonella (E.) typhosa* in 10 minutes, and a 1:12000 solution of available chlorine killed *Staphylococcus aureus* in 10 minutes. See table 3.

TABLE 3

BACTERICIDAL EFFICIENCY OF AVAILABLE CHLORINE EMPLOYING A MODIFIED F. D. A. METHOD AT 20° C.

Available Chlorine	*Salmonella (E.) typhosa* 10 minute contact	*Staphylococcus aureus* 10 minute contact
1:11000	0	0
1:12000	0	0
1:13000	0	+
1:14000	0	+
1:15000	0	+
1:16000	0	+
1:17000	+	+
1:18000	+	+
Phenol Control		
1:60	0	0
1:70	0	0
1:80	0	+
1:90	0	+
1:100	+	+
1:110	+	+

0 = No growth after 48 hours. + = Growth after 48 hours.

With a modified F. D. A. method, a 1:12000 solution of free iodine killed *Salmonella (E.) typhosa* in 10 minutes, and a 1:13000 solution of free iodine killed *Staphylococcus aureus* in 10 minutes. See table 4.

TABLE 4

BACTERICIDAL EFFICIENCY OF FREE IODINE EMPLOYING A MODIFIED F. D. A. METHOD AT 20° C.

	Salmonella (E.) typhosa	*Staphylococcus aureus*
Free Iodine	10 minute contact	10 minute contact
1:11000	0	0
1:12000	0	0
1:13000	+	0
1:14000	+	+
1:15000	+	+
Phenol Control		
1:60	0	0
1:70	0	0
1:80	0	+
1:90	0	+
1:100	+	+
1:110	+	+

0 = No growth after 48 hours. + = Growth after 48 hours.

A summary of the phenol coefficients of free iodine and available chlorine by the "Semi-micro" Method and a modified F. D. A. Method is recorded in table 5.

TABLE 5

"SEMI-MICRO" METHOD

Disinfectant	Test Organism	Phenol Coefficient
Available Chlorine	*Salmonella (E.) typhosa*	44
	Staphylococcus aureus	62
Free Iodine	*Salmonella (E.) typhosa*	89
	Staphylococcus aureus	75

MODIFIED F. D. A. METHOD

Disinfectant	Test Organism	Phenol Coefficient
Available Chlorine	*Salmonella (E.) typhosa*	177
	Staphylococcus aureus	171
Free Iodine	*Salmonella (E.) typhosa*	133
	Staphylococcus aureus	185

Summary

The Klarmann "Semi-micro" Method was used to determine the bactericidal efficiences of free iodine and available chlorine using 24 hour cultures of *Staphylococcus aureus* and *Salmonella (E.) typhosa* at 20°C. as the test organisms.

A modified F. D. A. method was used to determine the bactericidal efficiences of free iodine and available chlorine against 24 hour cultures of *Staphylococcus aureus* and *Salmonella (E.) typhosa* at 20°C.

Solutions containing available chlorine (2 percent) were prepared from sodium hypochlorite solution (5 percent). The free iodine solutions were prepared from Iodine Tincture (2 percent) U. S. P.

Conclusions

1. In Klarmann's "Semi-Micro" Method, the phenol coefficient of available chlorine was found to be 44 against *Salmonella (E.) typhosa* and 62 against *Staphylococus aureus.* With the same method, free iodine gave a phenol coefficient of 89 against *Salmonella (E.) typhosa* and 75 against *Staphylococcus aureus.*

2. In a modified F. D. A. method, the phenol coefficient of available chlorine was found to be 177 against *Salmonella (E.) typhosa* and 171 against *Staphylococcus aureus.* With the same method, free iodine gave a phenol coefficient of 133 against *Salmonella (E.) typhosa* and 185 against *Staphylococcus aureus.*

3. Iodine Tincture (2 percent) displays a high and effective bacteriocidal efficiency as revealed either by a modified F. D. A. technique or by the Klarmann "Semi-Micro" Method. In either procedure, this tincture reveals a marked safety factor as might occur in practice when it is diluted by body fluids.

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(4) Klarmann, E. G.: *Am. J. Pharmacy, 120*:321 (Sept., 1948).

(5) *United States Pharmacopoeia, Thirteenth Revision* (April, 1947), Mack Publishing Company, Easton, Penna.

EFFICIENCY OF THREE DIFFERENT IODONIUM COMPOUNDS AGAINST GRAM NEGATIVE BACTERIA

By Louis Gershenfeld and Conrad Kruse *

THE iodonium compounds are members of a class of compounds in which iodine as a part of a positive ion is present as an integral part of their structure. They are strong bases, and when neutralized with acids form stable salts. It is in this respect that they behave as do the quaternary ammonium and tertiary sulfonium compounds. They are decomposed on heating, thus resembling the "onium" derivatives (1).

Iodine, in its positive valency, has been under much investigation for the past half century. Most of the work during this time was primarily for the preparation of iodonium compounds.

First mention of iodine as a polyvalent ion was made by Willgerodt in 1885 (2). In 1893 Hartman and Meyer (3) discovered the existence of the iodonium compounds.

Recently Gershenfeld and Witlin (1) reported on the antibacterial activity and bacteriostatic efficiency of iodonium compounds. They reported that iodonium compounds, in powder form, displayed antibacterial activity and, in saturated aqueous solution, displayed bactericidal efficiency against *Staphylococcus aureus*.

Purpose

The purpose of this investigation was to study the effect of Bis (methyl phenyl) iodonium chloride, Bis (3,4 dichlorophenyl) iodonium chloride and Bis (2,4 dichlorophenyl) iodonium sulfate as antibacterial agents against gram negative bacteria.

Procedure

In both the bactericidal and bacteriostatic tests, six organisms were employed; namely, *Shigella alkalescens*, *Proteus vulgaris*,

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

Pseudomonas aeruginosa, Klebsiella pneumoniae, Salmonella enteritidis and *Neisseria catarrhalis.* The three compounds [1] tested were:

Bis (3,4 dichlorophenyl) iodonium chloride
approximate solubility in water 0.1%

Bis (2,4 dichlorophenyl) iodonium sulfate
approximate solubility in water 0.1%

Bis (methyl phenyl) iodonium chloride
approximate solubility in water 0.1%

Part I

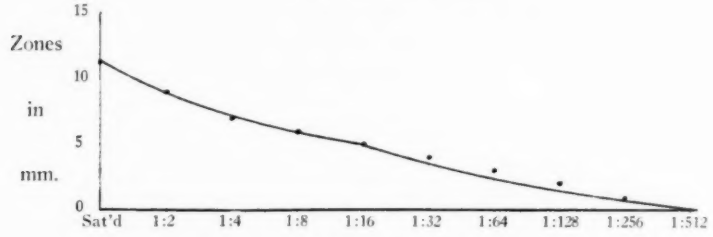
Testing for Bacteriostasis

Using the F. D. A. agar plate technic (4), the three compounds under study were tested against the six organisms.

A saturated aqueous solution was made of each of the iodonium compounds. They were prepared by taking an excess amount of the compound and placing it into a volumetric (100 ml.) flask. Sterile distilled water was then added to the mark. After thorough agitation this solution was then allowed to stand for twenty-four hours, after which it was filtered. The first portion through the filter paper was not collected.

The test organisms used were twenty-four hour F. D. A. broth cultures.

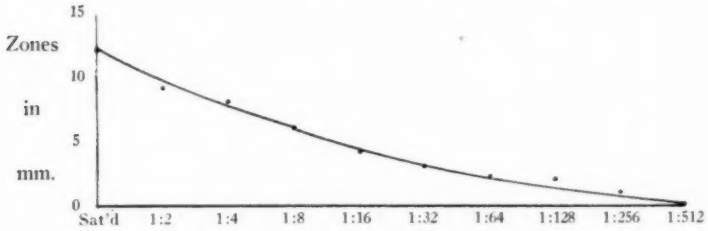
Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Shigella alkalescens*



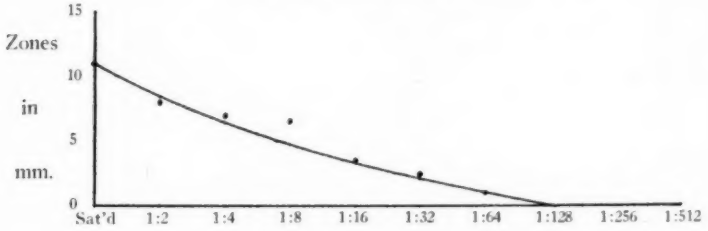
Bis (methyl phenyl) iodonium chloride

[1] The compounds were prepared, and their solubilities were determined by the Iodine Educational Bureau Project at Battelle Memorial Institute, Columbus, Ohio.

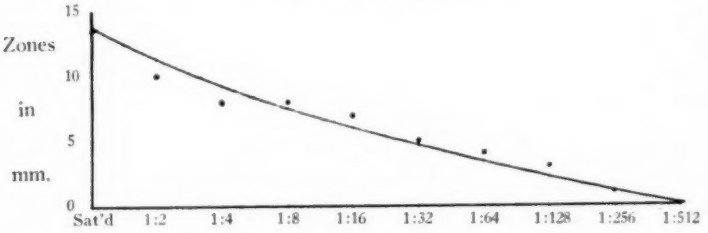
Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Proteus vulgaris*



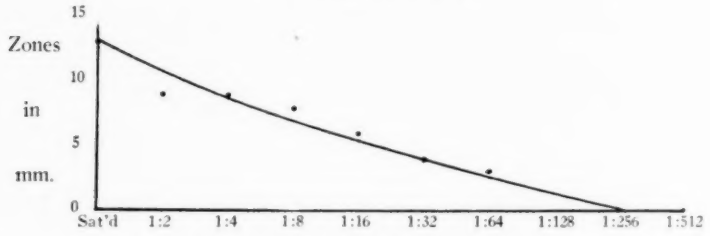
Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Pseudomonas aeruginosa*



Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Klebsiella pneumoniae*

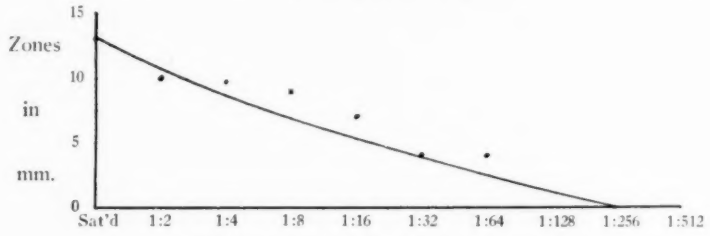


Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Salmonella enteritidis*



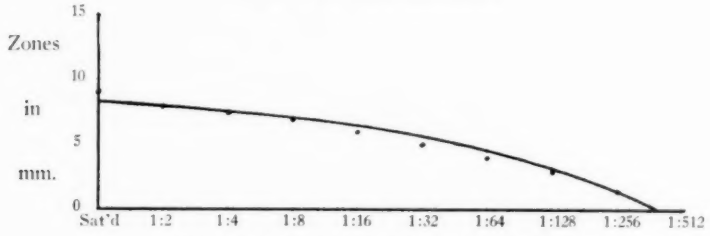
Bis (methyl phenyl) iodonium chloride

Zones of Inhibition Produced by Bis (methyl phenyl) iodonium chloride against *Neisseria catarrhalis*



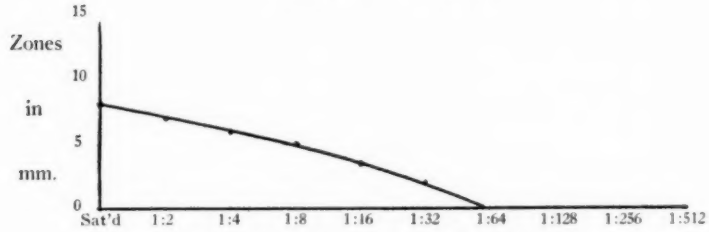
Bis (methyl phenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Shigella alkalescens*



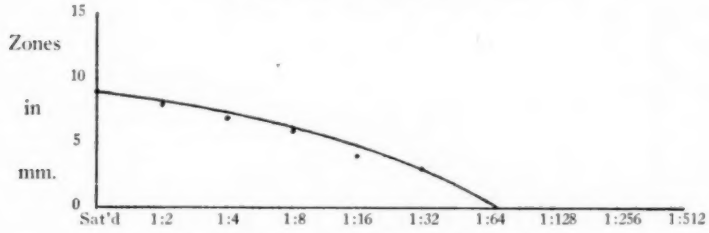
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Proteus vulgaris*



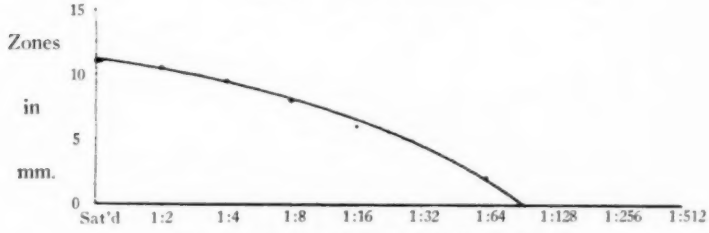
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Pseudomonas aeruginosa*



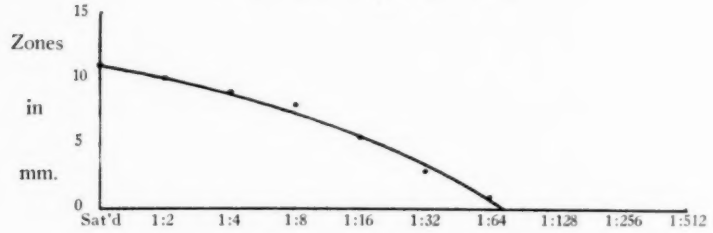
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Klebsiella pneumoniae*



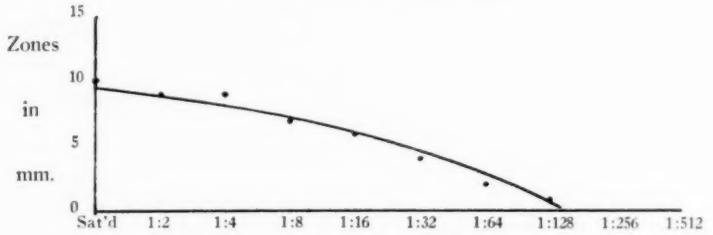
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Salmonella enteritidis*



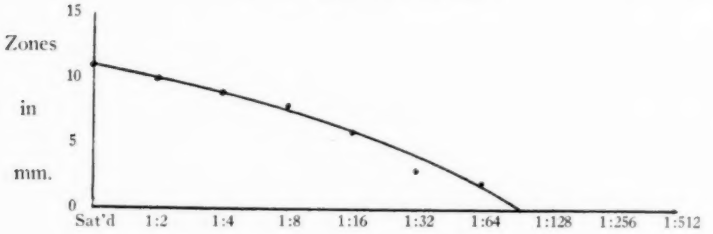
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (3,4 dichlorophenyl) iodonium chloride against *Neisseria catarrhalis*



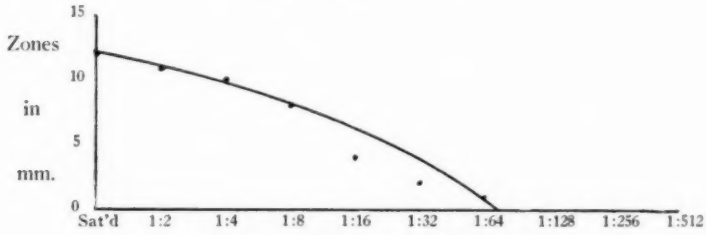
Bis (3,4 dichlorophenyl) iodonium chloride

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Shigella alkalescens*



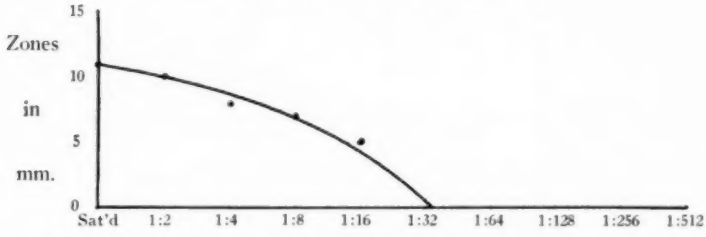
Bis (2,4 dichlorophenyl) iodonium sulfate

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Proteus vulgaris*



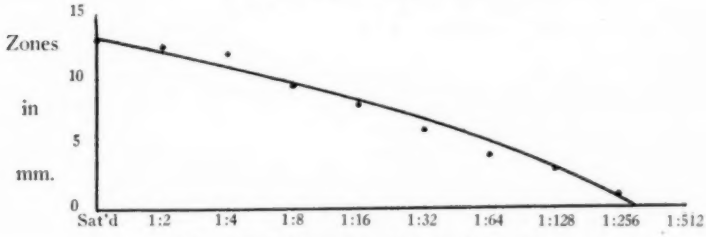
Bis (2,4 dichlorophenyl) iodonium sulfate

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Pseudomonas aeruginosa*



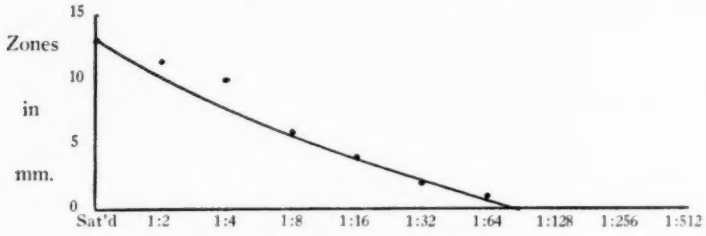
Bis (2,4 dichlorophenyl) iodonium sulfate

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Klebsiella pneumoniae*



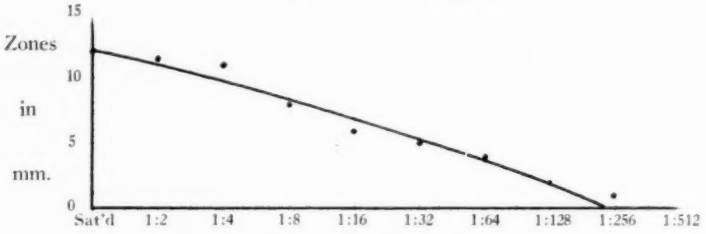
Bis (2,4 dichlorophenyl) iodonium sulfate

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Salmonella enteritidis*



Bis (2,4 dichlorophenyl) iodonium sulfate

Zones of Inhibition Produced by Bis (2,4 dichlorophenyl) iodonium sulfate against *Neisseria catarrhalis*



Bis (2,4 dichlorophenyl) iodonium sulfate

Part II

Bactericidal Efficiency

Bactericidal efficiencies of the three iodonium compounds were determined against the six test organisms, employing the F. D. A. Phenol Coefficient Technique. Dilutions of the iodonium compounds were made from saturated aqueous solutions. The findings follow:

Bis (methyl phenyl) iodonium chloride Dilutions	*Shigella alkalescens* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:5 saturated aqueous solution	+	+	+
1:10 " " "	+	+	+
Phenol 1:80	+	0	0

+ indicates growth. 0 indicates no growth.

Bis (methyl phenyl) iodonium chloride Dilutions	*Proteus vulgaris* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:5 saturated aqueous solution	0	0	0
1:10 " " "	+	+	+
Phenol			
1:100	+	0	0

Bis (methyl phenyl) iodonium chloride Dilutions	*Pseudomonas aeruginosa* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
1:20 " " "	+	+	+
1:30 " " "	+	+	+
Phenol			
1:75	+	0	0

Bis (methyl phenyl) iodonium chloride Dilutions	*Klebsiella pneumoniae* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:5 saturated aqueous solution	+	+	0
1:10 " " "	+	+	+
Phenol			
1:95	+	0	0

Bis (methyl phenyl) iodonium chloride Dilutions	*Salmonella enteritidis* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:5 saturated aqueous solution	+	0	0
1:10 " " "	+	+	+
Phenol			
1:90	+	0	0

Bis (methyl phenyl) iodonium chloride Dilutions	*Neisseria catarrhalis* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol			
1:90	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Shigella alkalescens* Minutes		
	5	10	15
1:20 saturated aqueous solution	0	0	0
1:30 " " "	+	+	0
1:40 " " "	+	+	+
Phenol			
1:80	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Proteus vulgaris* Minutes		
	5	10	15
1:20 saturated aqueous solution	0	0	0
1:30 " " "	+	0	0
1:40 " " "	+	+	+
Phenol			
1:100	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Pseudomonas aeruginosa* Minutes		
	5	10	15
1:5 saturated aqueous solution	0	0	0
1:10 " " "	+	0	0
1:20 " " "	+	+	+
Phenol			
1:75	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Klebsiella pneumoniae* Minutes		
	5	10	15
1:20 saturated aqueous solution	0	0	0
1:30 " " "	+	+	0
1:40 " " "	+	+	+
Phenol			
1:95	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Salmonella enteritidis* Minutes		
	5	10	15
1:20 saturated aqueous solution	0	0	0
1:30 " " "	+	0	0
1:40 " " "	+	+	+
Phenol			
1:90	+	0	0

Bis (3,4 dichlorophenyl) iodonium chloride Dilutions	*Neisseria catarrhalis* Minutes		
	5	10	15
1:10 saturated aqueous solution	0	0	0
1:20 " " "	+	+	0
1:30 " " "	+	+	+
Phenol			
1:90	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Shigella alkalescens* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol			
1:80	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Proteus vulgaris* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol			
1:100	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Pseudomonas aeruginosa* Minutes		
	5	10	15
Saturated aqueous solution	+	0	0
1:10 saturated aqueous solution	+	+	+
Phenol			
1:75	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Klebsiella pneumoniae* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol			
1:95	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Salmonella enteritidis* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol 1:90	+	0	0

Bis (2,4 dichlorophenyl) iodonium sulfate Dilutions	*Neisseria catarrhalis* Minutes		
	5	10	15
Saturated aqueous solution	0	0	0
1:10 saturated aqueous solution	+	+	+
Phenol 1:90	+	0	0

Summary

Three different iodonium compounds, Bis (methyl phenyl) iodonium chloride, Bis (3,4 dichlorophenyl) iodonium chloride and Bis (2,4 dichlorophenyl) iodonium sulfate, were tested for their antibacterial efficiency against six gram negative organisms. The F. D. A. agar cup plate was used to note bacteriostatic efficiency.

The bactericidal efficiency of the iodonium compounds against six organisms was determined by the F. D. A. Phenol Coefficient Technique (4).

The test bacteria were: Broth cultures (24 hours old) of *Shigella alkalescens, Proteus vulgaris, Pseudomonas aeruginosa, Klebsiella pneumoniae, Salmonella enteritidis* and *Neisseria catarrhalis.*

Conclusions

(1) Saturated aqueous solutions of the following iodonium compounds: Bis (methyl phenyl) iodonium chloride, Bis (3, 4 dichlorophenyl) iodonium chloride, and Bis (2,4 dichlorophenyl) iodonium sulfate displayed bacteriostasis. Inhibition zones ranged from 8 mm. to 13.5 mm.

The three compounds tested showed approximately equal zones of inhibition for each organism. In comparing the antibacterial ac-

tivity of the three compounds on the different organisms, *Pseudomonas aeruginosa* displayed the smallest zones and *Klebsiella pneumoniae* the largest zones of inhibition. *Shigella alkalescens, Proteus vulgaris, Salmonella enteritidis* and *Neisseria catarrhalis* were intermediate.

(2) Bactericidal efficiencies were displayed by Bis (methyl phenyl) iodonium chloride, Bis (3,4 dichlorophenyl) iodonium chloride and Bis (2,4 dichlorophenyl) iodonium sulfate against the six organisms. Of the three compounds tested, Bis (3,4 dichlorophenyl) iodonium chloride produced the greatest effect. Dilutions of 1:20 of a saturated aqueous solution had a bactericidal effect against the six organisms. The other two compounds were bactericidal only when used in a saturated aqueous solution.

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SOYBEAN OIL AND PROTEIN

By T. Swann Harding

THE soybean has been known from antiquity in China. The first written record of it occurs in a medical manuscript prepared by the Emperor Sheng Nung in 2838 B. C. Soybeans were grown in Pennsylvania as early as 1804. The Department of Agriculture began to introduce new varieties and later to breed varieties useful for specific purposes shortly before the turn of this century. But significant quantities were not grown here until about 1930, when the crop was 14 million bushels. Since then production has risen sharply, and it hit 181 million bushels in 1947.

This truly is a wonder or a miracle bean. The Chinese proved that, by putting it to multiple uses. Modern industry will prove it again in newer ways. Already we are becoming familiar with soybean oil in shortening, margarine, and salad oils and with protein-rich soybean meal as a component of flours for making more nutritious baked goods. But the industrial diversity and versatility of soybeans almost defy imagination.

The oil can be pressed out of soybeans or it can be extracted by using a solvent. In the first method the beans are reduced to suitable size by grinding, then heated and squeezed in huge presses from which the soybean oil drips. But the heat destroys the value of the protein for many purposes.

In the second method the beans are also converted to suitable size and shape but are then extracted with hexane, a petroleum product, which is percolated through the beans until all their oil is dissolved. The solution of the oil is then heated to recover the solvent.

Soybean oil is also soluble in alcohol when the mixture is heated. If ethyl alcohol is used instead of hexane, the oil settles out when the solution is cooled and can readily be drawn off. This oil is a glyceride containing four fatty acids which differ only in their number of hydrogen atoms.

The more unsaturated a fatty acid is the more readily it combines with oxygen. Acids containing 4 and 6 fewer than maximum hydrogen atoms—linoleic and linolenic—are particularly important in determining the ability of a vegetable oil to combine with oxygen; it is such a combination that makes a drying oil. The liquid oil film is thus converted into a tough resinous coating which is not sticky and does not rub off. Linseed oil is a drying oil, soybean oil is semi-drying, and olive oil is nondrying.

When dry, films of soybean oil are flexible rather than brittle; when exposed away from the sun, as on interior walls, they do not tend to become yellow. These qualities are much in demand for protective and decorative coatings, the flexibility ensuring long durability without cracking or chipping, and the nonyellowing being important when pastel colors are used for decoration. But a device is needed to hasten the drying rate and yet preserve the valuable characteristics of soybean oil.

The simplest is to mix it with a rapid drying oil like linseed or tung oil. Other methods involve chemical treatment—combinations with maleic anhydride, sorbic acid, or even sodium or copper—or heating with alkali, certain iodine compounds, or a mixture of nickel and carbon. In this instance improvement results, not via chemical combination, but from a change in the relative position within the unsaturated fatty acid molecule of the points where hydrogen-atom deficiencies occur.

Soybean oil can be converted into its fatty acids by saponification, and these then combined with other chemicals, glycerine or phthalic acid, for instance. The product is a synthetic resin widely used as a vehicle in interior wall paints and enamels and automobile finishes. But many difficulties remain, and scientists of the Department of Agriculture are working to solve them. In 1947, almost four times as much linseed as soybean oil was used to make paints, even though the former is derived from an imported and the latter from a domestic crop.

The most important single use of soybean oil is in paints and varnishes insofar as industry is concerned. Other uses which consume it in smaller quantities are the making of soap, linoleum, oilcloth, and printing inks. The use of soybean oil in the preparation of polyamide resins also stands out. These resins have been pro-

duced commercially for only a short time, but their unique properties have gained them wide acceptance. They make excellent adhesives and moisture-proof coatings for paper.

The modern point of view is to regard soybean oil as a raw material rather than a product. Then it must be converted into new and valuable products by chemical modifications. The new products will no doubt be more useful than any available today. The production of polyamide resins from soybean oil is an example. In preparing them the glycerol and certain fatty acids in the oil are obtained as by-products. The resins are chemically similar to nylon but have a different sphere of utility because of their own special properties. A wide variety of substances may be obtained, some of them with rubber-like properties.

Another line of study concerns the flavor of soybean oil as it is affected by different processing methods. As usually prepared it does not have a long storage life. The Germans had increased its storage life by adding a little citric acid during deodorization; this not only increases storage life but directly enhances flavor stability. A number of companies are now testing the method.

Since the processing operations are varied, samples of oil must be tested at various stages. The flavor can be measured only organoleptically by trained panels. An elaborate procedure has been developed for selecting, training, and utilizing such panels at the Northern Regional Research Laboratory in Peoria. The procedure evolved has been a distinct contribution to organoleptic evaluation methods. Several industrial companies have adopted it.

A great deal of work has also been done on the alcoholic extraction of soybeans at this same Department of Agriculture laboratory in Peoria. If the soybean flakes are extracted at the boiling point of 95-percent ethyl alcohol, it takes 6 parts of alcohol to 1 part of meal to do the job of dissolving out the oil; under pressure 1:1 mixtures can be used, thus saving a lot of alcohol. To recover the oil, the alcoholic extract merely has to be cooled to 60°F., whereupon the oil settles out. Then the reclaimed alcohol can immediately be used for another batch!

The soybean oil so separated contains about 7 percent of alcohol which is also recovered. The final oil contains a lower percentage of free fatty acids than the hexane-extracted product, and it is excellent

either for food uses or the production of paints. The solids which separate out in the cooling process consist of about 40 percent lecithin mixed with sterols, saponins, glycosides and other materials. The meal obtained has been debittered in the process, has a bland flavor, and is excellent for food use. The process has been thoroughly studied on a laboratory and pilot-plant scale and is now under commercial test.

The soybean meal obtained after alcoholic extraction of the flakes now yields very interesting products on water extraction; when 1 part of it is treated with 6 parts of water, 70 percent goes into solution. The solid matter can be recovered readily by spray drying, and 55 percent of it consists of protein, readily water-soluble. A solution of this product having a protein content of 5 percent or more will gel when heated to 194°F; this gel is irreversible and has the consistency of gelatin dessert.

The properties of this material closely approximate those of eggwhite, and are not similar to those of any other soybean product so far prepared. It has extremely interesting possibilities in both the food and industrial fields. For instance, it can be used as an adhesive for envelopes which cannot be steamed open; it would work as a seal either by remoistening or by heat. This seal also wets metal, making it possible, for instance, to seal a label directly to a can without having to overlap it as at present.

This soybean protein makes an excellent substitute for technical, non-edible eggwhite in the crown seal industry. Again, this process is under commercial test.

Water extraction of the hexane-extracted meal yields a protein-containing product which does not gel when heated in water solution. This is because the hexane-extracted meal contains a gel inhibitor. But this inhibitor, which readily dissolves in water, can also be removed by alcoholic extraction of the previously hexane-extracted meal.

A large cartridge manufacturing company was recently approached on the possibility of using these new adhesives in making shotgun casings. Because of the Peoria laboratory's background of experience the company asked it for suggestions on something to replace synthetic adhesives made from nonagricultural products. Experiments were made and the soybean-protein adhesive proved

admirable for this specific use. Thereupon commercial use of the method began.

Experiments on paint formulations, using soybean oil, have resulted in the development of a soybean oil paste, containing also the proper admixture of pigments and driers, now being marketed to farmers. It enables a farmer to produce an acceptable and durable paint at a relatively low cost by merely mixing it with soybean oil. This is the first 100-percent soybean oil paint to be a commercial success, and it was developed by the Peroria laboratory in cooperation with an outside concern. With 5 percent of lime in the pigment, it has been found that the 100-percent soybean oil paint coatings do not collect nor retain dirt.

Norelac is the new synthetic resin developed from soybean oil at the Northern Regional Research Laboratory. The soybean oil is modified chemically, and semicommercial trials are being made by a private concern. The resin is valuable as a heat seal in food packaging.

Great is the wonder bean, and this merely skims the surface of the subject.

SELECTED ABSTRACTS

Headaches Cured by Injections of Histamine. M. Eszenyi-Halasy. *Brit. Med. J.* No. 4616:1121 (1949). The author classified the largest group of patients who were treated in the study as having histamine headache. These were apparently caused by an accumulation of histamine causing an upset in cell metabolism. A test injection of 0.3 mg. of histamine would produce a typical headache. Other types of headache treated in the study were migraine, psychic, relaxation, alcoholic, hypertensive, and those having an organic origin.

Following the test dose of histamine the patient was given a series of desensitizing doses of histamine starting with a subcutaneous injection of 0.1 mg. After 3 or 4 such daily doses the tolerance of the patient toward histamine gradually increased, and so the dose was also gradually increased until 0.2 mg. was given. Of 80 patients treated 56 obtained complete cure or marked improvement. The duration of treatment varied, but many were cured within a few days. Four typical case histories were given. All of the patients had had headache of long duration which were resistant to all other methods of therapy. The author followed the cases after treatment for a minimum period of 6 months.

No severe side effects were observed in any case. A number of the patients experienced palpitations during the first few days of treatment, and several complained of a metallic taste in their mouth shortly after injection. A few patients experienced vomiting.

The author concluded that treatment with histamine is worthwhile in all cases of frequent headaches of long duration.

The Effect of Para-Aminosalicylic Acid on the Development of Streptomycin Resistance by the Tubercle Bacillus. O. E. Graessle and J. J. Pietrowski. *J. Bact. 57*:459 (1949). The development of streptomycin resistance by *Mycobacterium tuberculosis* during therapy reaches such a high level that compensation by

correspondingly increased dosage is not possible. Any subsequent therapeutic value of the antibiotic is also practically eliminated. The authors made a study of the effect of para-aminosalicylic acid on the development of resistance to streptomcyin *in vitro*. The human strain of *M. tuberculosis* was used in the tests.

The initial sensitivity of the organisms to streptomycin was 0.8 units per cc. of culture medium. Repeated exposure to the antibiotic resulted in a slow increase in resistance during the first 30 days but a rapid increase to 20,000 units per cc. by the end of 80 days. In comparison PAS was initially effective in a concentration of 1.0 mg. per cc., and exposure for 120 days failed to increase the resistance. When a combination of streptomycin and PAS were used, it was found that the organism was sensitive to 0.6 units of streptomycin and 0.3 micrograms of PAS per cc. Following 120 days of repeated exposure to the combination the bacteria were sensitive to 1 unit of streptomycin and 0.5 micrograms of PAS. Subsequent tests with each drug alone showed that the bacteria were still sensitive to the same degree as before exposure to the combination. Thus PAS prevented the development of streptomycin resistance by *M. tuberculosis in vitro*.

These findings cause hope to be held that low concentrations of PAS may prevent the development of streptomycin resistance *in vivo* as it did *in vitro*.

The Treatment of Infantile Gastroenteritis. C. Z. Neumann. *Brit. Med. J.* No. 4619:132 (1949). The etiology of infantile gastroenteritis is not clearly understood. A small portion of the cases are definitely infective in origin, particularly in tropical areas. However, an extensive study of the stools of healthy and diseased infants has revealed practically no difference in the flora. The author suggested that at least part of the symptomatology of the disease can be attributed to a manifestation of histamine intoxication.

Based upon this assumption the author treated a series of severely ill infants with benadryl in a dose of 1 mg. for each month of age at intervals of 4 hours. This dose interval was increased to 6 hours when improvement was evident. This dosage applied to infants up

to 5 months of age. From 6 months to 1 year the dose used was 6 to 8 mg. administered the same way. The number of stools decreased rapidly following the institution of antihistamine therapy, but the fever and toxic symptoms were often uninfluenced. However, when a sulfonamide was administered concurrently, the number of stools not only decreased rapidly but the clinical picture improved rapidly and permanently. The toxic manifestations such as vomiting, dyspnea, prostration, and tachycardia disappeared rapidly. The author favored the use of either sulfamezathine or phthalylsulfathiazole. Neither the benadryl alone nor the sulfonamide alone brought about as favorable results as did the combination.

The author postulated that, the beneficial action which has been recorded in literature for all types of therapeutic agents in the past, such as castor oil and pectin, and for the agents described in this report, may be attributed to the removal or neutralization of histamine by rapid evacuation, by adsorption, or through the direct action of antihistaminics. The action of the sulfonamides may be to inhibit the growth of pathogenic organisms and thus prevent the formation of histamine.

Penicillin-Resistant Staphylococci Susceptible to Aureomycin. D. R. Nichols and G. M. Needham. *Proc. Staff Meet. Mayo Clin. 24*:309 (1949). A study of the resistance of 50 strains of *Staphylococcus aureus* to penicillin, streptomycin, and aureomycin revealed startling facts. The strains were all isolated from clinical material. Of the 50 strains, *in vitro* tests proved that 34 were penicillin-resistant. More than 1.6 Oxford units of penicillin per cc. of culture medium were required to inhibit the growth of the organisms. Also, 14 of the 34 resistant strains required more than 25 mg. of streptomycin to inhibit growth. However, all of the strains were inhibited by as little as 0.78 mg. of aureomycin per cc. of culture medium. The same conditions were found in 15 strains isolated from staphylococcic bacteremia. Twelve of these strains were resistant to penicillin, 3 to streptomycin, but none to aureomycin in the concentrations used above.

Clinical trial of aureomycin resulted in cures of 4 of 6 cases of staphylococcic bacteremia which were resistant to penicillin. The

authors felt that a cure may have been attained in one of the other cases had not the supply of aureomycin been exhausted. Initially the aureomycin was administered to 4 of the patients intravenously. The dosage employed ranged from 200 to 500 mg. in 250 cc. of saline solution administered every 4, 6, or 12 hours. For the completion of the treatment in these 4 and in the other 2 cases, the antibiotic was given orally. The dosage employed by this route were 500, 750, or 1000 mg. administered every 4 or 6 hours.

The case of one patient illustrates the effectiveness of aureomycin in these cases of bacteremia. The patient had received one million units of penicillin intramuscularly each day for 9 days without benefit. Penicillin was discontinued and aureomycin begun. The aureomycin was given intravenously for 24 hours at the rate of 500 mg. every 6 hours. Then for 5 days the aureomycin was given at the rate of 500 mg. every 4 hours, orally. The patient's temperature was normal within 24 hours, and his blood culture was negative within 48 hours. Recovery from the infection was complete.

The Effect of Rutin on the Biological Activity of Vitamin C. E. W. Crampton and L. E. Lloyd. *Science 110:*18 (1949). The biological potency of vitamin C in certain vegetable sources has been found to be greater than the chemical assay of the ascorbic acid content of those vegetables would indicate. A preliminary report by the authors of a study to investigate this phenomenon was presented in the indicated journal.

A total of 96 guinea pigs were maintained on a diet devoid of ascorbic acid, except for the known quantities of the vitamin administered as a supplement to the diet. The animals were divided into three groups. The supplement of one group was crystalline ascorbic acid, of the second group was canned orange-grapefruit juice, and of the third group was dehydrated potatoes. The ascorbic acid levels fed to each group were 0.5, 0.79, 1.26, and 2.00 mg. Half of the animals in each group also received 100 mg. of crystalline rutin per day. Using the odontoblast method of assaying biological activity, it was found that the animals receiving rutin had significantly higher values on the response-dose curve at the lower three dosage levels.

This enhanced biological value of vitamin C noted in these tests was apparently due to the presence of rutin. The mode of action of rutin is not known, but certain possibilities were suggested by the authors. There is the possibility that rutin makes more ascorbic acid available at the lower dosage levels, or it may delay *in vivo* destruction of the vitamin. Another possibility is that rutin forms the basis for the synthesis of additional ascorbic acid by the animal body. This latter possibility is suggested by the similarity between the glucose-fructose side chain of the rutin molecule and the structure of ascorbic acid. The presence of rutin in certain natural vitamin C sources may be the factor which has enhanced the biological potency of the vitamin in these sources.

The Treatment of Radiation Sickness With Desoxycorticosterone Acetate. F. Ellinger, B. Roswit and S. M. Glasser. *Am. J. Roentgenol. and Radium Therapy 61:*387 (1949). Previous investigations with animals, particularly the demonstration that desoxycorticosterone acetate protects the liver against irradiation-induced fatty changes, formed the rational basis for the clinical use of this drug in the treatment of radiation sickness. A series of 50 patients were studied and the results presented in this preliminary report. The patients were all irradiated for a variety of benign and malignant conditions and were suffering with nausea and vomiting as well as with other symptoms of radiation sickness. The radiation dosage varied from 50 r, to a total cumulative dose of 7500 r.

Each patient received 5 mg. of desoxycorticosterone acetate in peanut oil intramuscularly every 8 hours. Administration continued until there was a relief of symptoms but for a period of not longer than 5 days. This attempt to avoid overdosage prevented the development of untoward reactions to the drug in all of the patients. In those cases in which radiation sickness recurred during continued irradiation a second therapeutic series was given following an interval of 3 to 5 days.

Only 3 of the 50 patients failed to obtain a response to this hormone, and those requiring additional therapeutic series obtained relief with each series. Two of the 3 failures occurred in patients suffering

from inoperable advanced brain tumors. Of the 47 patients relieved 37 were completely relieved of the most distressing symptoms, nausea and vomiting.

Desoxycorticosterone acetate, therefore, seems to be clinically effective in the relief of radiation sickness. The authors felt that the particular results obtained in those patients in whom the field of irradiation included the liver were noteworthy in that they corroborated the animal experimentation in which it was found that this hormone prevented the roentgen-ray induced fatty changes in the liver. Thus it was felt that the hormone strikes at the etiological factor producing radiation sickness.

BOOK REVIEWS

Blakiston's New Gould Medical Dictionary, 1st Edition. Edited by H. W. Jones M. D.; N. L. Hoerr M. D., Ph. D.; and A. Osol Ph. D. 1294 pages; 252 illustrations, 129 in color. The Blakiston Co., Philadelphia and Toronto; 1949. Textbook Edition $8.50, Deluxe Edition $13.50.

This entirely new medical dictionary is without doubt an outstanding achievement in its field. Its three chief editors were assisted by an editorial board with Dr. Morris Fishbein acting as editorial consultant.

Its scope embraces the fields of medicine, dentistry, pharmacy, nursing and veterinary medicine, as well as their many supporting basic sciences. Over 80 contributors aided in the selection of words and terms for inclusion, and a most comprehensive coverage has been attained.

The format and type used are very easy to follow and read, with each defined word in bold face type so that it can be quickly found. Phonetic spelling of each word follows, making it a simple matter to learn its pronunciation. Word sources are given, and each definition is clear and concise with all nuances of use explained, as well as obsolescences.

A special section is devoted to tables of important data for ready reference, and an atlas containing 252 illustrations is bound in the center of the book. Of these a large number are color plates, and the coloring is excellent.

One is impressed, upon examining this new dictionary, with the thoroughness with which the editors and their contributors have accomplished this great task. It is a *new* dictionary in every sense of the word, and there seems no doubt but that it will receive wide and enthusiastic acceptance by both workers and students in the many fields that it covers.

L. F. Tice

Freedom From Want—A Survey of the Possibilities of Meeting the World's Food Needs. A Symposium. Edited by E. E. De Turk for the American Association for the Advancement of Science. 80 p. illustrated *Chronica Botanica 11*, No. 4 (1948). The Chronica Botanica Co., Waltham, Mass. Price $2.00.

This number of *Chronica Botanica* represents the published papers of six eminent authorities who participated in a seminar on this subject arranged by the Agriculture Section of the American Association for the Advancement of Science in December 1946.

A foreword by Norris E. Dodd, Director-General, Food and Agriculture Organization of the United Nations is followed by:

Population and Food Supply by H. R. Tolley;

World Soil and Fertilizer Resources in Relation to Food Needs by R. M. Salter;

Crop Production Potentials in Relation to Fredom from Want by K. S. Quisenberry;

Animal Production in an Efficient Food Economy by F. B. Morrison;

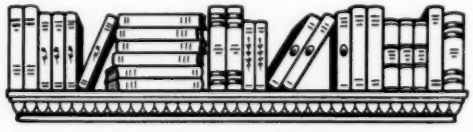
The Economics of Freedom from Want by J. D. Black; and,

Obligations of Science Toward Freedom from Want by M. A. McCall.

A number of illustrations are included in this compilation including a symbolic frontispiece "Ceres".

Those interested in the current race between food production and population increase will find this compilation of interest. The contributors are obviously not of the Malthusian school, and optimism seems their keynote.

L. F. Tice



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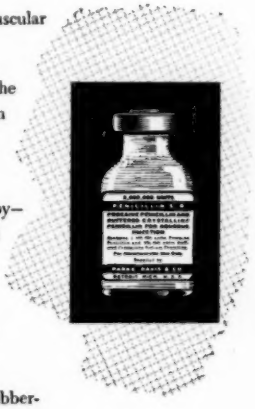

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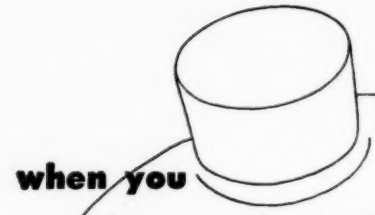

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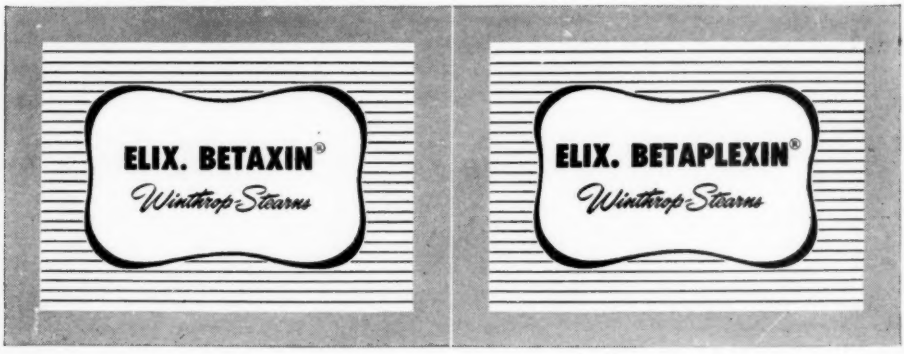

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